

3. (Amended) The method of claim 1, further comprising the step of partitioning the population of RNA molecules before providing the population of cDNA molecules.

4. (Amended) The method of claim 1, wherein said cDNA population is derived from the 5' ends of the RNA molecules.

5. (Amended) The method of claim 1, wherein said cDNA population is derived from the interior regions of the RNA molecules.

6. (Amended) The method of claim 1, wherein said cDNA population is derived from the 3' ends of the RNA molecules.

7. (Amended) The method of claim 1, wherein said partitioning step optionally comprises hybridizing a probe nucleic acid sequence to the population of nucleic acids.

9. (Amended) The method of claim 1, further comprising ligating adapter oligonucleotides to the termini of the digested cDNA molecules, thereby producing ligation products.

10. The method of claim 9, further comprising amplifying the ligation products.

11. (Amended) The method of claim 10, further comprising separating the amplified products.

12. The method of claim 11, wherein said separating is by gel electrophoresis.

13. (Amended) The method of claim 11, wherein the first nucleic acid sequence is identified by comparing the size of one or more digestion products produced by a member of the subpopulation of nucleic acid sequences to the sizes of fragments generated by the same restriction enzyme or enzymes in said reference nucleic acid or nucleic acids.

14. The method of claim 11, further comprising
recovering one or more size-separated digestion products;
reamplifying the recovered products; and
separating the reamplified products.
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15. (Amended) The method of claim 14, wherein said separating is by gel electrophoresis or liquid chromatography.
16. (Amended) The method of claim 15, wherein the first nucleic acid sequence is identified by comparing the size of one or more digestion products produced by a member of the subpopulation of nucleic acid sequences to the sizes of fragments generated by the same restriction enzyme in said reference nucleic acid sequences.
17. (Amended) The method of claim 9, further comprising:
inserting the ligation product into a cloning vector to form a vector-insert;
transforming the vector-insert into a suitable host;
culturing the host under conditions allowing for replication of the vector-insert;
recovering the vector-insert from said host; and
digesting the vector-insert with one or more restriction enzymes, thereby releasing said insert; and
comparing the size of the insert to sizes of fragments generated by the same restriction enzyme or enzymes in said reference nucleic acid or nucleic acids.
18. (Amended) The method of claim 1, wherein at least a portion of the first nucleic acid sequence is determined and compared to nucleotide sequence to the nucleotide sequence of one or more reference nucleic acid sequences.

19. (Amended) The method of claim 1, wherein the determining step comprises hybridizing the first nucleic acid sequence to one or more of the reference nucleic acid sequences.

20. (Twice Amended) A method for equalizing the representation of nucleic acid sequence in a population of nucleic acid sequences, the method comprising in order the steps of:
providing a population of cDNA molecules derived from a population of RNA molecules, wherein said cDNA population comprises a first nucleic acid and a second nucleic acid sequence having a nucleic acid sequence distinct from the first nucleic acid sequence, and wherein said first nucleic acid sequence is present at a higher level in said population than said second nucleic acid sequences;

partitioning said cDNA population into one or more subpopulations of nucleic acid sequences,

wherein said partitioning comprises digesting the cDNA population with one or more restriction enzymes; and

lowering the level of said first nucleic acid sequence relative to the level of said second nucleic acid sequence in the subpopulation of nucleic acid sequences, thereby equalizing the representation of nucleic acid sequences in said population of nucleic acid sequences.

27. (Amended) The method of claim 1, wherein the partitioning step optionally comprises one or more processes selected from:

- a) isolating nucleic acid sequences from different cell types;
- b) separating the nucleic acid sequences in the subpopulation by physical properties;
- c) amplification of a specific subpopulation of nucleic acid sequences;
- d) amplifying 5' terminal sequences of the nucleic acid sequences;
- e) amplifying interior sequences of the nucleic acid sequences; and
- f) amplifying 3' terminal sequences of the nucleic acid sequences;
- g) partitioned subtraction screening,
- h) mass spectroscopy,
- i) length selection by lariat formation,
- j) use of identical primers,
- k) use of shortened primers,

- l) use of intermediate annealing temperature,
- m) use of modified cycle times, and
- n) incremental batch assembly.

28. (Amended) A method of identifying a novel nucleic acid sequence, the method comprising:

providing a population of nucleic acid molecules;

normalizing the population to provide one or more subpopulations of nucleic acid sequences;

sequencing a plurality of nucleic acid sequences in the one or more subpopulations;

assembling the plurality of nucleic acid sequences to provide an assembled sequence; and

determining whether the assembled sequence is absent in a reference set of one or more reference nucleic acid sequences;

whereby if the assembled sequence is absent from the reference the set assembled sequence is a novel nucleic acid sequence.

29. The method of claim 28, wherein the normalizing comprises partitioning.

30. (Amended) The method of claim 29, wherein the partitioning comprises one or more processes selected from:

- a) isolating nucleic acid sequences from different cell types,
- b) separating the nucleic acid sequences in the subpopulation by size,
- c) amplification of at least one subpopulation of nucleic acid sequences,
- d) amplifying 5' terminal sequences of the nucleic acid sequences,
- e) amplifying interior sequences of the nucleic acid sequences,
- f) amplifying 3' terminal sequences of the nucleic acid sequences, and
- g) hybridization of said population against a prepared library of known nucleotide sequences;
- h) partitioned subtraction screening,
- i) mass spectroscopy,
- j) length selection by lariat formation,

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- k) use of identical primers,
 - l) use of shortened primers,
 - m) use of intermediate annealing temperature,
 - n) use of modified cycle times, and
 - o) incremental batch assembly.
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32. (Amended) A method of screening a population of nucleic acid molecules to identify a novel sequence, the method comprising:

providing a population of nucleic acid sequences;

CF normalizing said population into one or more subpopulations of nucleic acid sequences, wherein said normalizing is selected from the group consisting of restriction endonuclease digestion, size-based fragment partitioning; terminal nucleotide sequence, and fragment migratory pattern;

identifying a first nucleic acid sequence in the subpopulation of nucleic acid sequences; and

comparing the first nucleic acid sequence to a reference nucleic acid sequence or sequences, wherein the absence of the first nucleic acid sequence in the reference nucleic acid sequence or nucleic acid sequences indicates the first nucleic acid sequence is a novel nucleic acid sequence.

Add new claim 33:

CF 33. The method of screening as in claim 33 wherein the normalization step comprises processes selected from the group consisting of partitioned subtraction screening, mass spectroscopy, length selection by lariat formation, use of identical primers, use of shortened primers, use of intermediate annealing temperature, use of modified cycle times, use of a 5'-capped end and incremental batch assembly.

Pursuant to 37 CFR 1.121(c)(1)(ii), a marked up version of the claims showing the changes made appears as Appendix A of this Amendment.